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Clinical Toxicology

Anicteric hepatitis and uveitis in a worker exposed to trichloroethylene

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Summary: A previously healthy woman developed acute anicteric hepatitis which slowly resolved, though bilateral anterior uveitis then appeared. No other cause than an occupational exposure to trichloroethylene was found, and rechallenge by resuming work has led to a transient increase in serum alkaline phosphatase. Both manifestations may constitute a rare systemic reaction to trichloroethylene.

Introduction

Trichloroethylene ($CHCl:CCl_2$) is widely used as an industrial solvent and its metabolism and toxicity have been extensively studied.[1] Exposure is usually by inhalation, whence it is rapidly absorbed showing high solubility in adipose tissue and slow elimination, mostly through the lungs in unchanged form. Since trichloroethylene has a rather long biological half-life,[2] its cumulative effects must be considered, together with those of its principal metabolic products - trichloroacetic acid, and trichloroethanol.[3] Central nervous system and cardiac toxicity are the most important adverse effects in both acute and chronic poisoning,[1,4] but liver injury is not definitely established in occupational exposures. Animal experiments have demonstrated that large, near-fatal acute doses are required to produce mild hepatic dysfunction.[5] However, repeated bouts of acute exposure were found to lead to cirrhosis or the development of hepatocellular carcinoma in National Cancer Institute tests on mice.[6] In humans, the ability of trichloroethylene to produce hepatic cell necrosis and fatty liver was suggested[7,8] but there are few reports on its hepatotoxicity in chronic occupational exposures, and a systemic reaction is exceedingly rare. We report an acute toxic hepatitis associated with bilateral anterior uveitis, in a worker exposed to trichloroethylene.

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Case report

A previously healthy 48 year old woman was admitted with a 5-day history of anorexia, recurrent painless vomiting, and fever (38.5°C). Her physical examination was normal. Laboratory tests were as follows: ESR 112 mm/hour (Westergren), haemoglobin 10.9 g/dl with normal indices, white cell count 8.3×10^9/l with left shift and eosinophilia (475, later 820 cells) and platelets 472×10^9/l. Urinalysis and serum glucose, urea and electrolytes were normal. Serum alkaline phosphatase was 490-609 IU/l (normal <120), transaminases 70-100 IU/l (normal <33), 5'nucleotidase 38-52 IU/l (normal <14) with normal serum amylase, bilirubin, proteins, electrophoresis, prothrombin time was normal but later decreased to 60% of control (7 seconds). Cholesterol and triglyceride were normal. Repeated cultures and extensive serological testing were negative, including negative hepatitis A and B as well as Epstein-Barr virus and cytomegalovirus serology. No autoantibodies were found. Electrocardiogram, chest X-ray and abdominal imaging by computed tomographic scan and ultrasound were normal. There was no history of alcohol consumption or the use of any drugs.

Occupational history revealed chronic exposure to trichloroethylene vapour, used as a solvent in the factory where she worked for several years. Her job included cleaning parts with trichloroethylene in a cold bath for about 3 hours per day. In addition, she was in the vicinity (6 m) of a heated trichloroethylene tank used for degreasing, which had no fume hood (exposure of between 25% and 75% of an 8-hour working day). The patient was not exposed to other organic solvents or hepatotoxins.

Industrial hygiene samples for trichloroethylene were only rarely obtained at the time, and ranged from 40 ppm to 800 ppm (8-fold the permissible exposure level).

The patient declined a liver needle biopsy and was discharged for ambulatory follow-up with a recommendation for rest and no specific treatment. At home, vomiting soon resolved and low fever persisted for another week and then abated. Marked lassitude and anorexia continued however, and were associated with a weight loss of 4 kg/month and the appearance of palmar erythema. Then, slow symptomatic recovery took place over 6 weeks with a gradual but complete normalization of *all* blood tests (the serum alkaline phosphatase being last to return to normal levels). At that time, pain and blurred vision appeared in both eyes and bilateral anterior uveitis was diagnosed and treated successfully by topical corticosteroids and mydriatics. Gastrointestinal X-ray studies were ordered at that time but showed no abnormality. Six months after her illness commenced and when complete symptomatic and biochemical recovery was established, a rechallenge was made by the patient's return to her previous work. Within 2 weeks lassitude reappeared as well as an isolated significant increase in serum alkaline phosphatase. At that time air sampling for trichloroethylene revealed exposure of 550 ppm and trichloroacetic acid was discovered in the patient's urine. The patient was transferred to office duties where she has been entirely well during a follow-up period of over one year.

Discussion

Our patient presented with an acute onset of hepatitis with no prodrome, associated with several 'systemic' manifestations such as fever, markedly elevated ESR, eosinophilia and the later development of bilateral anterior uveitis, which may also be related. The increase in serum alkaline phosphatase/5'nucleotidase (× 4–5) and aminotransferases (× 3) suggests a combination of intrahepatic cholestasis and liver cell necrosis, while the associated phenomena are not uncommonly observed to accompany liver injury by immunological reaction to a drug.[8] No definite aetiology could be established for both conditions but the history of occupational exposure to trichloroethylene, the absence of any other underlying disease or causative factor, the spontaneous recovery and the flare following rechallenge by the patient's resuming her previous work – all support trichloroethylene toxicity as the underlying mechanism. Furthermore, diseases resembling 'vinyl chloride disease' – an entity characterized by multi-system involvement and the participation of immune mechanisms[9] have been observed after exposure to trichloroethylene.[10] Thus, the reported case suggests that, though a rare occurrence, both anicteric hepatitis and anterior uveitis may constitute a sensitization reaction to trichloroethylene in susceptible individuals and may follow chronic exposure in an industrial setting.

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